

SPL ER/DL Team

May 25, 2011

Minutes

Teleconference information:

USA Toll-Free 866-213-2145

Access code: 273 8216

Chair for this meeting: Jessica Dunn Skorupski

1. Pillbox Initiative Update – Jess

- Federal register notice came out this week.
- NLM has project – website to identify solid dosage forms and provide links to related labeling.
- <http://pillbox.nlm.nih.gov>
- Voluntary program to create images for your products that can be added to SPL and thus posted to the NLM. We don't know when/if this will become mandatory.
- We are trying to get Pillbox representatives to come to SPL team forums to answer questions.
- Expected process:
 - Sponsors would supply samples of drug to NLM for photographing.
 - NLM would take photographs – very exact standards /specifications. There will also be an encryption within the image so that the validation program can determine that it is a legitimate image taken by NLM.
 - Images would be provided back to sponsors for review/confirmation
 - Sponsors would then include the image in SPL file
 - Images would then be included in the pillbox web site
- There is currently a reference to the product image in the SPL implementation guide.
- Samples of the actual product will be destroyed by NLM.

2. Drug Listings - Marilyn

- a. For All API shipped to the US from a foreign facility, the drug listing must include .jpegs of the Bulk Drum Label that contains the foreign manufacture's NDC code (Labeler code-product code-**) and the drug listing information (minus the Content of Labeling)
 - See the wiki for the FDA instructions on how to create this SPL
 - Document type: Bulk ingredient
 - Marketing category: Bulk ingredient
 - No content
- b. For Bulk shipped Drug Product what is required (i.e. .jpeg of bulk drum label and drug listing information [minus the content of labeling] because the manufacturer NDC's are assigned and are different from the distributor NDC's included in the Content of Labeling. Or if the Content of Labeling were include, the manufacturer's NDC's would then be added to the Content of Labeling or substituted?
 - Document type: Bulk ingredient
 - Marketing category: Drug for further processing
 - Data elements: enter all information as if it were a finished product
 - NO NDA number
 - Maximum number of capsules that can be in the bulk drum.
 - This should NOT appear on Daily Med.
 - Teva sent one in and it was posted on Daily Med --
 - Fluoxetine capsule/TevaCanada Limited.

- c. For Finished Packaged Drug Product by a foreign manufacturer, would the Content of Labeling need to include the manufacturer's NDC's or just be listed in the drug listing section. Also would the .jpegs be the distributor's labels and/or cartons?
- We've sent this question to DLRS for the minutes
 - Teva has recently submitted one of these. Ruth Kirkner
 - Document type: Human Drug Product
 - Marketing category: Approved product -- made exclusively for PLD
 - Paul Loebach said to use the label of the actual finished product in the PLD section.
3. The PLR revision date is located at the end of the Highlights section. This date at the end of the Highlights section is also deemed by FDA SPL schema to be the SPL Effective Time (ET). Therefore, the SPL ET changes upon every SPL version...and must. However, the PLR revision date located at the end of the Highlights section is expected to identify the enclosure or package insert revision date. Has anyone else run into a problem with this? We received a letter from FDA asking us to change the SPL ET to be the PLR revision date, but we cannot. Has this issue been addressed previously? Is Lonnie aware? – Jean
- Lonnie is aware.
 - This is actually a question back to the review division.
 - Resolution: Educate the review. Reply back to the review division that this date carries over directly from the SPL. We have no control over this date. If they need further information on SPL, they should call Lonnie Smith.
 - The effective date in the SPL can be the same as the previous version. The version number needs to increase when a new SPL is submitted.
 - Many sponsors put text in the bottom of the content of labeling that shows the literature revised date
4. Does an SPL submission with a future date go through all the same validations as a file with a current market start date? - Jean
- Yes
 - This date should be very far in the future.
5. Mismatched addresses between DFARS and D&B are being flagged now. How can we manage these mismatches of suppliers? – Jean
- Sponsors are responsible for contacting CM to have the supplier change their address.
 - The DRLS group is also contacting establishments to facilitate corrections.
 - Rationale: FDA wants to be able to have a clean supply chain that they can potentially inspect.
 - If you think that this is a D&B issue, let the SPL group know and they will try to help.
- *****
6. Please discuss the suggestion of including lot distribution data in the SPL file. How can this be accomplished? Will an SPL file have to be updated at each lot release? – Jean
7. We currently use the campus approach for our manufacturing facility at our corporate center. We are currently trying to assess the possibility (and value) of subdividing the campus into smaller sub-sites, based on manufacturing functional -- ie API, dry products, and parenteral. - Pat

8. Are companies adding alternate testing sites for drug substances to the Labeler and Manufacturer Information section of the SPL or just adding the API supplier to the Labeler and Manufacturer Information section of the SPL? – Kathleen
9. Has anyone received the following packaging validation error even though there are no drug listing differences in the SPL since the last posted SPL: "If the NDC Package Code has been previously submitted, then the package form code and quantity value and unit must be the same as in the most recent submission for this NDC code". – Amy
10. In a situation where a CBE is changed to a PAS, and the CBE version of the circular is pulled back and replaced with the previous version while the PAS is pending, what is the process for replacing the eListed SPL with the previous version? Can we revert back to the previous SPL version we already submitted? Or do we need to resubmit that SPL as a new version with new version number and rootID? Also, is there a defined period of time after a CBE is submitted that FDA has to tell a sponsor to change a CBE to a PAS? - Amy
11. There are two examples of Drug Listing Data for products that use the term "equivalent to" and want to see how other companies are portraying this information. - Kathleen
Have seen similar "equivalent to" information in labels and see other companies portray this information different than our company does:
- a. Example 1: Description section states, "Each mL contains 118 mcg of dexmedetomidine hydrochloride equivalent to 100 mcg of dexmedetomidine". Drug Listing Data looks like this:
- Active Ingredient/Active Moiety:
Ingredient Name: **DEXMEDETOMIDINE HYDROCHLORIDE** (Dexmedetomidine)
Basis of Strength: Dexmedetomidine
Strength: 100 ug in 1 mL
- In this case does it matter whether you use 118 mcg/mL and choose dexmedetomidine hydrochloride as the basis of strength?
- b. Example 2: Description section states, "The vials contain sterile vancomycin hydrochloride equivalent to either 500 mg or 1 g vancomycin activity.". Drug Listing Data looks like this
- Active Ingredient/Active Moiety:
Ingredient Name: **VANCOMYCIN HYDROCHLORIDE** (VANCOMYCIN)
Basis of Strength: VANCOMYCIN
Strength: 500 mg in 10 mL or 1 g in 20 mL
- In this case does it matter whether you use 118 mcg/mL and choose dexmedetomidine hydrochloride as the basis of strength?
12. My boss is expressing concern over these new document types (I thought I was going to have to give her CPR). Lonnie has requested that we switch our Kogenate antihemophilic factor (recombinant) to the plasma derived template. The templates listed below will be available in the newest i4i release set for June 5th. Please see her comments below.

New SPL Document Types

- CELLULAR THERAPY
- CELLULAR THERAPY with highlights

- PLASMA DERIVATIVE
- PLASMA DERIVATIVE with highlights
- LICENSED VACCINE BULK INTERMEDIATE LABEL
- LICENSE BLOOD INTERMEDIATES/PASTE LABEL
- STANDARDIZED ALLERGENIC
- STANDARDIZED ALLERGENIC with highlights

"To have any classification or categorization of recombinant products as plasma-derived products without a recombinant distinction can be quite problematic. As the SPL is posted publicly, can be downloaded by anyone with access to the internet, yet can easily misinterpret the evolving and complex data associated with these files, it is of great concern that someone could misunderstand that this recombinant product is somehow also viewed as a plasma-derived product. This immediately brings to mind the valid concerns and problems of plasma-derived products during the 1990s where some used plasma containing infectious disease elements before certain infectious diseases were better understood. There are countries that depend upon the FDA-associated documentation of US approved biologics, yet are only beginning to introduce recombinant products into their countries.

The below statement is from the FDA - CBER website on a project page "Towards More Effective Treatment for Blood Clotting Disorders: Pharmacogenetics of von Willebrand Factor (vWF) and Related Proteins":

<http://www.fda.gov/BiologicsBloodVaccines/ScienceResearch/BiologicsResearchAreas/ucm127059.htm>

The Division of Hematology is responsible for the evaluation of biologic products related to blood. Among these products are recombinant coagulation factors that are substitutes for their plasma-derived counterparts.

If it is a matter of naming a document type or template, please consider adding "recombinant" or changing to "factors". Please do not limit the name to 'plasma derived'."

Followup with outcomes:

- Paula Finn: problems with establishment information for "campuses" and French.